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Analysis of RAS-mutation and microbiom of patients with colorectal cancer

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Abstract

© 2018, Advanced Scientific Research. All rights reserved. In Russia, over the past 50 years, the number of primary diseases with colorectal cancer (CRC) has increased 7-fold; today in Tatarstan every 42nd resident of the republic is registered as an oncological patient. Analysis of patients with diagnosed rectal cancer in the RT revealed that the overall incidence of KRAS mutations was 33%, 68% of cases with mutations in the 12th codon, 33% of the detected mutant KRASs are homoduplexes. Patients older than 60 years carry the mutant KRAS, which nullifies the effectiveness of Epidermal Growth Factor receptor (EFGR) inhibitors, in only 10% of cases. In the group of patients younger than 50 years, KRAS mutations were found in 58.3% of cases. The microbial profile of the biopsy specimens revealed a tendency for phylum Bacteroides and Enterobacteriaceae to predominate on intact epithelium and replace them with tumor genera Faecalibacterium, Streptococcus and Fusobacterium on tumor. The taxonomic structure of bacterial communities of biopsy specimens is diverse; in tumor tissue, diversity can both decrease and increase. The representation of the Prevotella genus in the epithelium with the mutant KRAS gene was increased in 50% of cases. Expanding the spectrum of molecular targets in the epithelium and intestinal microbiome should ensure the effectiveness of personified antitumor therapy.

Keywords

Colorectal cancer, High-resolution melting method, KRAS, Metagenomic sequencing, Microbiome

References

[1] P. Larki, E. Gharib, M. Yaghoob Taleghani, et al. “Coexistence of KRAS and BRAF Mutations in Colorectal Cancer: A Case Report Supporting The Concept of Tumoral Heterogeneity”, Cell J, 2017, vol.19, №1, pp.113-117.

[2] Genetics of Colorectal Cancer (PDQ): Health Professional Version. 2002-2018. PDQ Cancer Genetics Editorial Board. PDQ Cancer Information Summaries. Bethesda (MD): National Cancer Institute (US).

[3] A. Zehir, R. Benayed, R.H. Shah, et al. “Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients”, Nat Med, 2017, vol.23, № 6, pp.703-713

[4] Y.Y. Chang, P.C. Lin, H.H.Lin, et al. “Mutation spectra of RAS gene family in colorectal cancer”, Am. J. Surg., 2016, vol.212, №3, pp.537-544.

[5] D. Ciliberto, N. Staropoli, F. Caglioti, et al. “The best strategy for RAS wild-type metastatic colorectal cancer patients in first-line treatment: A classic and Bayesian meta-analysis”, Crit. Rev. Oncol. Hematol., 2018, vol.125, pp.69-77.

[6] P.M. Wilson, M.J. Labonte, H.J. Lenz “Molecular markers in the treatment of metastatic colorectal cancer”, Cancer J., 2010, vol.16, №3, pp.262-72.

[7] Boleij, V. Tack, A. Taylor, et al. “RAS testing practices and RAS mutation prevalence among patients with metastatic colorectal cancer: results from a Europe-wide survey of pathology centres”, BMC Cancer, 2016, vol.16, №1, pp.825.

[8] F. Guo, H. Gong, H. Zhao, et al. “Mutation status and prognostic values of KRAS, NRAS, BRAF and PIK3CA in 353 Chinese colorectal cancer patients”, 2018, Sci. Rep. vol.8,№1, pp.6076.

[9] F.D. Faleel, M.I. Zoysa, M.D. Lokuhetti, et al. “Modified mismatch polymerase chain reaction-restriction fragment length polymorphism detected mutations in codon 12 and 13 of exon 2 of K-ras gene in colorectal cancer patients and its association with liver metastases: Data from a South Asian country”, J. Cancer Res. Ther., 2016, vol.12, №4, pp.1272-1277.

[10] M. Levi, G. Prayogi, F. Sastranagara, et al. “Clinicopathological Associations of K-RAS and N-RAS Mutations in Indonesian Colorectal Cancer Cohort”. J. Gastrointest. Cancer, 2018, vol.49,№2, pp.124-131.

[11] N Amirifard, E. Sadeghi, N. Farshchian, et al. “Evaluation of KRAS Gene Mutations in Metastatic Colorectal Cancer Patients in Kermanshah Province”, Asian Pac J Cancer Prev., 2016, vol.17,№7, pp.3085-3088.

[12] N Mohsen, S. Ahmadreza, H. Fatemeh, et al. “Frequency of K-RAS and N-RAS Gene Mutations in Colorectal Cancers in Southeastern Iran”, Asian Pac. J. Cancer Prev., 2016, vol.17,№9, pp.4511-4515.

[13] I.G. Gataullin, M.G. Gordiev, R.K. Shakirov, et al. “Clinical evaluation of the K-RAS gene mutation in patients with colorectal cancer”. Volga Cancer Journal, 2016, Vol.3, No.25, p. 85-88.

[14] H. Tilg, T.E. Adolph, R.R. Gerner, et al. “The Intestinal Microbiota in Colorectal Cancer”, Cancer Cell, 2018, S1535-6108(18)30072-2.

[15] Q. Wang, L. Li, R. Xu “A systems biology approach to predict and characterize human gut microbial metabolites in colorectal cancer”, Sci Rep., 2018, vol.8,№1, pp.6225.

[16] O.N.Ilinskaya, V.V. Ulyanova, D.R. Yarullina, et al. “Secretome of Intestinal Bacilli: A Natural Guard against Pathologies”, Front Microbiol., 2017, vol.8, pp.1666.

[17] The state of cancer care provided to the population of Russia in 2016. 2017. Ed. A.D. Kaprin, V.V. Starinskii, G.V. Petrova. M.: FSBI “P.A. Hertsen Moscow Cancer Research Institute, branch office of FSBI “NMRRC””, Ministry of Health of Russia.

[18] V. Deschoolmeester, C. Boeckx, M. Baay, et al. “KRAS mutation detection and prognostic potential in sporadic colorectal cancer using high-resolution melting analysis”, British Journal of Cancer, 2010, vol.103,№10, pp.1627-1636.

[19] B. Flemer, D.B. Lynch, J.M. Brown, et al. “Tumour-associated and non-tumour-associated microbiota in colorectal cancer”. Gut., 2017,vol.66,№4, pp.633-643.

[20] Sobhani, J. Tap, F. Roudot-Thoraval, et al. “Microbial dysbiosis in colorectal cancer (CRC) patients”, PLoS One, 2011, vol.6,№1, pp.16393.

[21] G.D. Wu, J. Chen, C. Hoffmann, et al. “Linking long-term dietary patterns with gut microbial enterotypes”, Science, 2011, vol.334,№6052, pp.105-108.

[22] Z Dai, O.O. Coker, G. Nakatsu, et al. “Multi-cohort analysis of colorectal cancer metagenome identified altered bacteria across populations and universal bacterial markers”, Microbiome, 2018, vol.6,№1, pp. 70.

[23] M. Lopez-Siles, M. Martinez-Medina, R. Surís-Valls, et al. “Changes in the Abundance of Faecalibacterium prausnitzii Phylogroups I and II in the Intestinal Mucosa of Inflammatory Bowel Disease and Patients with Colorectal Cancer”, Inflamm. Bowel Dis., 2016, vol.22,№1, pp.28-41.

[24] C.V. Ferreira-Halder, A.V.S. Faria, S.S. Andrade “Action and function of Faecalibacterium prausnitzii in health and disease”, Best. Pract. Res. Clin. Gastroenterol., 2017, vol.31,№6, pp.643-648.

[25] D. Rea, G. Coppola, G. Palma, et al. “Microbiota effects on cancer: from risks to therapies”. Oncotarget, 2018, vol.9,№25, 17915-17927.

[26] S. Bullman, C.S. Pedamallu, E. Sicinska, et al. “Analysis of Fusobacterium persistence and antibiotic response in colorectal cancer”, Science. 2017, vol.358,№6369, pp.1443-1448.

[27] C. Tropini, K.A.Earle, K.C.Huang et al. “The Gut microbiome: connecting spatial organization to function”, Cell Host Microbe, 2017, vol.21, pp.433-442.

[28] N.T. Nguen, R.R. Vafin, I.V. Rzhanova et al. "Molecular genetic analysis of microorganisms with intraepithelial invasion isolated from patients with colorectal cancer." Molecular genetics, Microbiology and Virology, 2016, Vol.1, p. 22-27.